REMARKS/ARGUMENTS

Claims 1 to 5, 9 to 29, 62 to 70 and 72 are pending in this application. Claims 6 to 8, 30 to 61, 71 and 73 are canceled. Claims 10, 13, 19, 21, 23, 25, 26, 28, 64, 68, 69 and 70 are currently amended. Applicant believes that this amendment includes no new matter.

The Examiner objects to claims 10 and 71. Claim 71 is objected to as being in improper dependent form. Claim 71 has been canceled. Claim 10 is objected to because it recites "hereof". Claim 10 has been amended to delete "hereof".

The Examiner rejects claims 1 to 5, 7, 9 to 29 and 62 to 72 under 35 USC 112, first paragraph, as failing to comply with the enablement requirement. Applicant traverses the rejection.

The Examiner acknowledges that it is an art recognized problem of producing monoclonal antibodies at low yield. The Examiner points to lines 17 to 19 at page 2 of the specification which discuss the deficiencies in monoclonal antibody production by hybridomas which include low yield. Also mentioned in the preceding paragraph (lines 13 to 16, page 2 of the specification) are the excessive cost, expenditures and labor involved in the hybridoma method which, to a significant degree, are avoided by the present invention. The Examiner states that the specification is not enabled for the claimed method to produce a heterologous antibody in vitro, as instantly claimed, because the specification does not contemplate using a culture of transfected avian oviduct cells in vitro for producing antibodies and the specification's only contemplated use for transfected oviduct cells is in the context of producing a bird that would then produce eggs that express the heterologous antibody. Applicant disagrees.

First, the specification clearly enables the production of heterologous antibodies in oviduct cells in culture as can be seen in Example 1. Second, although an important aspect of the specification is for the production of transgenic birds, the invention is not limited thereto, as can be seen from the Examples section which clearly discloses methods of making antibodies in cell culture and, for example, page 60, line 6 to page 61, line 21, where production of antibodies in avian cells in culture is discussed. In addition, applicant wishes to draw the Examiner's attention to originally filed claim 1 in the case which states as follows:

1. A method for the production of an antibody by an avian cell comprising culturing an avian cell transfected with at least one expression vector comprising a transcription unit having a nucleotide sequence encoding an immunoglobulin polypeptide operably linked to a transcription promoter and a transcriptional terminator, and wherein the cultured avian cell produces an immunoglobulin polypeptide capable of forming an antibody. (underlining added by applicant for emphasis)

Clearly the production of antibodies in cell culture was not only contemplated and enabled but was an important aspect in the specification since originally filed claim 1, which is part of the specification, specifies producing antibodies using cultured avian cells. It should be noted that "culturing an avian cell" is understood in the art as a cell in culture growth medium and not a cell in a transgenic animal. Therefore, it cannot be correctly stated that the specification's only contemplated use for transfected oviduct cells is in the context of producing a transgenic bird. In fact, there is nothing in the specification that suggests that oviduct cells in culture which produce antibody are useful for producing transgenic avians and applicant is unaware of any such use.

The Examiner states that the specification does not teach the method step of isolating the immunoglobulin as claimed. Applicant disagrees.

Purification of antibodies was well known in the art at the time of filing. Antibody purification is a particularly easy task when isolating the antibody from growth medium. See for example, Kohler & Milstein, 1975, *Nature* 256: 495-497, which is cited in the specification (see, the paragraph beginning at line 13, page 1 of the specification). In addition, standard antibody isolation methodologies which employ use of protein A and protein G columns were well known in the art at the time of filing. In addition, purification methods are available such as those disclosed in the specification at page 61, lines 11 to 14 where it is stated that: "the individual immunoglobulin polypeptide may have peptide regions that are suitable for the isolation of the immunoglobulin polypeptide as, for example, a polyhistidine peptide for binding to a Ni^{+}-containing column." In

brief, antibody purification from growth medium is a straightforward task that could be accomplished by a practitioner of skill in the art at the time of filing.

The Examiner indicates that the instant invention fails to address the art recognized problem of low antibody yield. Applicant submits that there is no requirement for patantablity that applicant overcome the specific art recognized problem of low antibody yield. The use of avian oviduct cells in culture to make antibodies is a functional and useful method and as such is entitled to patent protection.

One such use, to which the invention is not limited, that would be apparent to a practitioner of ordinary skill in the art, is for the production of human Mabs having an oviduct cell avian glycosylation pattern which can allow for testing efficacy of the Mab on an experimental scale. This can be done before investing the time and resources required for the production of a transgenic avian which produces the mAb at high yield. Such testing can be particularly useful when assessing the value of a transgenic avian designed to produce the heterologous antibody in the egg white for packaging into an egg, in which case the heterologous antibody would be produced by oviduct cells in the transgenic avian.

The amount of antibody produced in the recombinant cultured oviduct cells of Example 1 may have been lower than that produced in the chicken embryo fibroblast cells of Example 3; however, antibody is produced at detectable levels in the oviduct cells and as such the recombinant antibody can be recovered at sufficient levels from the growth medium into which it is secreted by purification using standard methodologies.

The Examiner rejects claims 1 to 5, 7, 9 to 29, 62 to 72 under 35 USC 112, first paragraph, as failing to comply with the written description requirement. The Examiner states that the specification does not provide sufficient written description for "variants" of viral vectors and "variant thereof" of an immunoglobulin heavy chain variable region and an immunoglobulin light chain variable region. Applicant traverses the rejection.

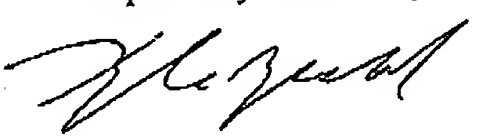
Applicant believes that the specification and the knowledge of a practitioner of skill in the art does provide for an adequate written description with regard to use of the term "variant" in the claims. However, to facilitate prosecution the claims have been amended to eliminate the specific use of the term "variant" with the caveat that a certain amount of variability can be present in viral vectors and immunoglobulin heavy chain

and light chain variable regions and as such certain variants are inherently within the scope of the claimed invention.

The Examiner rejects claims 7, 25, 28, 64 to 72 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner points to claims 7, 13, 25, 28, 64, 65 and 68 to 70, each as being unclear for certain reasons. To make the subject matter of the claims more clear, applicant has amended the claims to comply with the Examiner's comments regarding the clarity of the claims. Claim 7 has been canceled. Claim 13 has been amended to make clear that the constitutively active promoter is a cytomegaloviral promoter. Claims 25 and 28 have been amended to make clear that the claims are not directed to a mammal or an avian. Claims 23 and 26 have also been amended to add clarity. Claim 64 has been amended to make more clear that the avian cell cultured is an avian oviduct cell and that CTLA4 antibodies are produced by the cells. Claim 65 has been amended to make more clear that the nucleotide sequence is part of the expression vector. Claim 68 has been amended to specify that the claim is a method claim. Claim 69 and 70 have been amended to make more clear that the cell is an oviduct cell.

In conclusion, applicant submits that the claims 1 to 5, 9 to 29, 62 to 70 and 72 are allowable and respectfully requests the Examiner to pass the above-identified application to allowance.

Respectfully submitted,



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